Remarks

An Office Action was mailed in the above-captioned application on February 15, 2007. Claims 1-24 were pending. The Specification was objected to. Claims 1-20 and 24 were rejected under 35 U.S.C. 102(e) and under 35 U.S.C. 103(a). Claims 21-23 were withdrawn from consideration.

This Amendment and Remarks document is submitted in response to said Office Action. Applicant respectfully requests reconsideration of the application, withdrawal of all objections and rejections, and allowance of the application in view of the amendments and remarks below.

Objection to the Specification

The Examiner has maintained the objection to the specification for the incorporation of "essential material" by reference to a publication. In particular, the "essential material incorporated by reference is the identification of what constitutes suitable prodrugs of loxapine." Office Action at 2.

"Essential material" is material that is necessary to satisfy the requirements of the first, second or sixth paragraphs of 35 U.S.C. § 112. *See* 37 CFR 1.57(c)(1)-(3); MPEP 608.01(p). The specification states "[t]he use of salts or prodrugs of the active ingredient can provide effective means for providing the appropriate amount of loxapine or amoxapine, respectively, to the subject, and may provide advantages in formulating, packaging, or otherwise preparing and/or administering the active ingredients." Paragraph [0015]. Furthermore, the specification states that "[i]n addition to salt forms, the present invention provides active compounds in a prodrug form. Prodrugs of the compounds described herein are those compounds that readily undergo chemical changes under chemical, biochemical or physiological conditions to provide loxapine or amoxapine, respectively. For example, prodrugs of loxapine or amoxapine include compounds that can be hydrolyzed, oxidized, hydrogenated, cleaved or otherwise reacted under biological conditions, in vitro or in vivo, to produce the active compound. Some phosphonooxymethyl prodrugs of loxapine are disclosed in Krise et al., J Pharm Sci. (1999) 88:922 and 928 and J Med Chem. (1999) 42:3094." Paragraph [0020]. Thus, Applicant submits that the specification provides the necessary support for the claims under 35 U.S.C. § 112. The Krise et al. references are provided because they disclose examples of prodrugs of loxapine.

Those of skill in the art are familiar with prodrugs and, in view of the teachings of the specification, would know how to make and use the same.

Applicant respectfully requests that this rejection be withdrawn.

The Amendments to the Claims

Claims 1, 5-9 and 11-20 have been amended and claims 2-4 have been cancelled. The amendments to the claims set forth above are fully supported by Applicant's originally filed specification and claim set, and no new matter has been added to the application as a result of the above claim amendments.

Claim Rejections Under 35 USC § 102

The Examiner has maintained the rejection of claims 1-3 and 10-15 under 35 USC 102(e) as being anticipated by Dehaven et al. (WO 02/060870). Office Action at 2-4.

As amended, claim 1 is directed to a "method for treating headache" and requires "administering to a subject in need of headache relief, an effective amount of a compound selected from the group consisting of loxapine, pharmaceutically acceptable salts of loxapine, and prodrugs of loxapine." This method is not disclosed by Dehaven et al. Accordingly, claim 1, and claims 2-3 and 10-15 which depend on claim 1, are not anticipated by Dehaven et al.

Reconsideration is respectfully requested.

Claim Rejections Under 35 USC § 103

The Examiner has maintained the rejection of claims 1-9 and 24 under 35 U.S.C. 103(a) as being unpatentable over Burns et al. (U.S. Patent No. 5,284,133). Office Action at 4-6.

In the previous Office Action, mailed June 2, 2006, the Examiner stated that Burns et al. teaches that many drugs, including analgesics, could advantageously be delivered by aerosol inhalation. The Examiner also interpreted a passage in Burns et al. as teaching that loxapine hydrochloride was a known headache analgesic. (June 2, 2006, Office Action at 8, lines 19-20). The Examiner concluded that "[i]t would have been apparent to a person of ordinary skill in the art at the time of the instant invention that one could utilize Burn's inhalation device to deliver loxapine hydrochloride in the practice of a method of treating pain, because [Burns et al. teaches]

loxapine hydrochloride is a known headache analgesic" (*Id.* at 9, lines 11-14).

However, the passage cited by the Examiner does not teach that loxapine hydrochloride is a known headache analgesic. The passage merely lists a variety of drug classes ("neuroleptics, psychotropics, narcotic antagonists, other central nervous system (CNS) drugs and headache analgesics") and then lists variety of drugs ("such as proclorperazine, fluphenazine hydrochloride, chlorpromazine, trifluperazine hydrochloride, thioridazine hydrochloride, loxapine hydrochloride, and haloperidol decanoate") as part of a long sentence concerning drugs for which there may be a tendency of some patients to overdose themselves. Burns et al., col. 7, lines 12-28.

Applicant submits that the passage may be fairly interpreted as teaching the listed drugs belong to one, or perhaps more than one, of the listed classes. However, it is inappropriate either to interpret this passage to mean that *each* of the listed drugs belongs to *each* of the listed drug classes, or to select one of the listed drugs and assign it to one of the listed categories. Interpreting this passage to teach that loxapine hydrochloride is a known headache analgesic would be like interpreting the phrase "fruits, vegetables, other produce and meats, such as pork, apples, potatoes, and squash" to teach that squash was a known meat. Clearly, this is not a rational interpretation. Furthermore, it ignores the interpretation the passage would be given by one of skill in the art. The Drug Information Handbook, 2nd edition, cited by the Examiner, for example, refers to loxapine's "onset of neuroleptic effect" (Drug Information Handbook, at 555; emphasis added). Applicant notes that "neuroleptics" is the first drug class listed in the passage cited by the Examiner. Applicant submits that the selection of the drug "loxapine hydrochloride" from among the various listed drugs, and assigning it to the class "headache analgesics" from among the various listed classes, was based not on the teachings of Burns et al, but rather on the teaching of Applicant's specification. It is impermissible, however, to engage in a hindsight reconstruction of the claimed invention using Applicant's specification as a template and selecting elements from a reference.

Claims 5 and 9 further require that the headache is a "migraine headache." Significantly, later in the same sentence cited by the Examiner, Burns et al. excludes loxapine hydrochloride from the list of drugs in the class of "migraine headache analgesics" (col. 7, lines 25-27). Thus, if anything, Burns et al. should be interpreted as teaching that loxapine hydrochloride is not a

drug for the treatment of migraine headache. Thus, for at least this additional reason, claims 5 and 9 are not obvious over Burns et al. because Burns et al. teaches away from using loxapine hydrocholoride for the treatment of migraine headache.

Burns et al. fails to teach or suggest the use of loxapine hydrochloride in the treatment of headache, as claimed by Applicant. Thus, the Examiner has failed to establish a *prima facie* case of obviousness, as each and every element of claims 1-9 and 24 is not taught or disclosed by Burns et al.

The Examiner has maintained the rejection of claims 10-15 as being unpatentable over Burns et al. in view of the Drug Information Handbook, 2nd edition. The Examiner acknowledges that Burns et al. lacks teaching of loxapine dosages, but asserts that these are supplied by the Drug Information Handbook. As discussed above, Burns et al. fails to disclose the use of loxapine for the treatment of headache. The Drug Information Handbook, does not cure this deficiency. In fact, the Drug Information Handbook, indicates that loxapine is used for the treatment of psychotic disorders, giving no indication that the drug could be used in the treatment of headache. Drug Information Handbook at 554.

Burns et al. in view of the Drug Information Handbook fails to teach or suggest the use of loxapine in the treatment of headache. Thus, for at least this reason, the Examiner has failed to establish a *prima facie* case of obviousness, as each and every element of claims 10-15 is not taught or disclosed by Burns et al. in view of the Drug Information Handbook.

Moreover, the dosages taught by the Drug Information Handbook are for the treatment of psychotic disorders. *See, e.g.*, Drug Information Handbook at 555 ("10 mg twice daily, increase dosage until psychotic symptoms are controlled") (emphasis added). These dosages taught by Drug Information Handbook to treat psychotic symptoms would not convey to one of skill in the art what dosages are appropriate to treat headache. See specification at paragraphs [0024]-[0025].

Thus, at least this additional reason, claims 10-15 are not obvious over Burns et al. in view of the Drug Information Handbook.

The Examiner has maintained the rejection of Claims 16-17 and 19-20 as being

unpatentable over Burns et al. in view of Nguyen et al. As discussed above, Burns et al. fails to disclose the use of loxapine for the treatment of headache. Nguyen does not overcome this deficiency. Nguyen discloses loxapine in its known role as an anxiolytic, but not in the treatment of headache.

Burns et al. in view of Nguyen fails to teach or suggest the use of loxapine in the treatment of headache. Thus, for at least this reason, the Examiner has failed to establish a *prima facie* case of obviousness, as each and every element of claims 16-17 and 19-20 is not taught or disclosed by Burns et al. in view of Nguyen.

The Examiner has maintained the rejection of Claims 16-18 as being unpatentable over Burns et al., in view of Rabinowitz et al. As discussed above, Burns et al. fails to disclose the use of loxapine for the treatment of headache. Because Rabinowitz et al. does not overcome this deficiency, the Examiner has failed to establish a *prima facie* case of obviousness, as each and every element of claims 16-18 is not taught or disclosed by Burns et al. in view of Rabinowitz et al.

Reconsideration is respectfully requested.

Double Patenting

The Examiner has maintained the rejection of Claims 1, 16-17, and 19 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 7, 9, 10, 12, and 13 of U.S. Patent No. 6,716,416.

The Examiner has maintained the provisional rejection of Claims 1 and 16-20 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 12, 15, 16, and 18 of copending Application Serial No. 10/653,876, and Claims 1 and 7-9 of copending Application Serial No. 10/633,877. Applicant believes that the Examiner intended to reject Claims 1 and 16-20 over copending Application Serial No. 10/633,876, not 10/653,876.

Applicant hereby agrees to file in this application Terminal Disclaimers with regard to U.S. Patent No. 6,716,416 and U.S. Patent Application Serial Nos. 10/633,876 and 10/633,877.

Conclusion

Applicant believes that the pending claims, as amended above, are in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to Deposit Account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-5117.

Respectfully submitted,

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